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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,495	01/20/2006	Frank C. Barone	PU60406	9754

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 08/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/565,495	BARONE ET AL.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☒ Claim(s) *1 and 6-8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/20/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Information Disclosure Statement

The information disclosure statement (IDS) submitted on January 20, 2006, has been considered and acknowledged.

Specification

The amendment to the specification has been received and the disclosure to the claims claiming priority to the application a 371 National Phase entry of international application number PCT2004/023658 filed July 22, 2004 which claims priority to U.S. Application No. 60/489,202 filed July 22, 2003 has been entered and acknowledged.

Claim Objections

Claim 1 is objected to because of the following informalities: The abbreviation LXR should be spelled out upon first use. Appropriate correction is required.

Claims 6-8 are objected to because of the following informalities: Each claim must end with a period. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

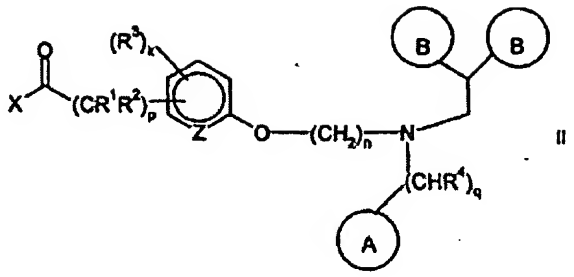
Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for cardiac hypertropy, does not reasonably provide enablement for coronary heart disease, arrhythmia, restricted coronary blood flow

arteriosclerosis, heart failure and myocardial infarction. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2nd 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

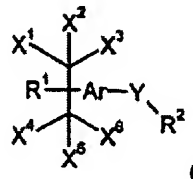
The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

1) Nature of the invention.

The nature of the invention is methods of preventing cardiovascular comprising administering a therapeutically effective amount of Liver X receptors (LXR) agonist or a pharmaceutically acceptable salt or physiologically function thereof. As stated, however, claim 1 recite that any or large representation of cardiovascular pathology is



intended with compounds of the or



(I)

shown structure is capable of cardiovascular pathology disorders.

2) State of the prior art and the predictability or lack thereof in the art.

Applicants' specification (see page 32) indicates large number unknown agents (e.g., protein factors, peptides, nucleic acids, natural compounds, or synthetic compounds) for discovering a candidate drug involves repeating the same test for several screening of a hundreds to several million times. This requires a great deal of reproducibility from the test. In order to obtain the state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibited the desired pharmacological activities (i.e. what compounds can treat which specific disease). The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher,* 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the

more specific enablement is necessary in order to satisfy the statue. Further, their mode of action is often unknown or very unpredictable and administration of the drugs can be accompanied by undesirable side effects.

Thus, in the absence of a showing of correlation between a representative number of the diseases claimed as capable of being treated by compounds of the instant claims, one of skill in the art is unable to fully predict possible results from the administration of the compounds due to the unpredictability of the role of the disease.

3) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The quantity of experimentation needed is undue experimentation as mentioned above. One of skill in the art would first need to determine the type of cardiovascular pathology disorders to be treated, and then determine which of the thousands of compounds of the above compounds would be suitable for said treatment and/or prevention.

4) Amount of direction and guidance provided by the inventor.

No working example is given on how the drug compound works in a patient. The claim is directed to treating neurodegenerative and or neuropsychiatric disorders in patient. The amount of direction or guidance present is found on pages 38-45 wherein *in vitro* assay was used to identify and evaluate growth of new neurons (nerogenesis). In addition, the gap between *in vitro* activity and *in vivo* utility is large enough to warrant thorough and compelling *in vivo* or clinical data. Notwithstanding this statement, on page 42 of the specification Applicant uses the phrase would be administered thus indicating the uncertainty of the claimed invention.

5) Existence of working examples.

Applicant's limited working example does not enable one of ordinary skill in the art to treat the numerous amounts of diseases encompassed by the instant invention with the numerous variation of the compounds supra.

6) Breadth of claims.

Claim 1 is extremely broad due to the vast number of possible diseases encompassed by the instant invention and the vast number of possible variation of the compound.

7) Level of ordinary skill in the art.

The level of ordinary skill in the art is high. Due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from its activity.

Hence, the specification fails to provide sufficient support of the broad use of the compounds of the claims for the prevention of a representative numbers of disease in claims 1-4. As a result necessitating one of skill in the art to perform an exhaustive search to determine which diseases can be treated by what compounds of the instant claims in order to practice the claimed invention.

Therefore, in view of the Wands factors, and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of ordinary skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compounds encompassed in instant claims, with no assurance of success.

The above list is by no means complete, but demonstrates the extraordinary breadth of causes, mechanisms, and treatment (or lack thereof) for cardiovascular pathology. It

establishes that it is not reasonable to any agent(s) to be able to treat cardiovascular pathology generally.

II. Claim 1-4 and 7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a written description rejection.

A lack of adequate written description issue arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967).

An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.

A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]."

In other words, the Applicant has not described with sufficient clarity a LXR agonist in the above mentioned claimed, nor described the pharmaceutically acceptable salt or carriers are described nor exemplified and does not inform the public of the limits of the monopoly asserted. Examiner suggest the incorporation of formula II or II a will overcome this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

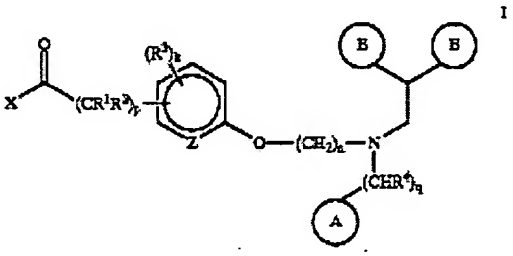
A person shall be entitled to a patent unless –

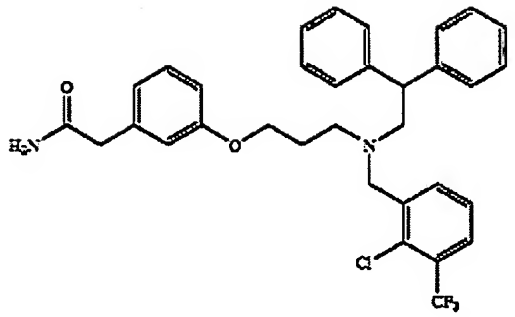
(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3 and 5-6 are rejected under 35 U.S.C. 102(a) and (e) as being anticipated by Collins et al. US 2005/0282908 A1

The applied reference has a common Assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

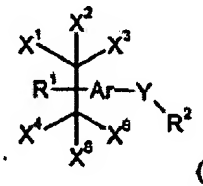
Collins et al. teach a LXR compound (as in claim 1) (see page 1 para. 0005) of formula  I structurally identical to the claimed formula of claim 5, having the same substituents (see para. 0006-0023) resulting in the

claimed LXR agonist compound  as in claim 6, treating cardiovascular diseases (see para. 0004) in pharmaceutically acceptable salt and a pharmaceutically acceptable carrier (see para. 0027) as in claim 3 administered in an effective amount (see para 0028).

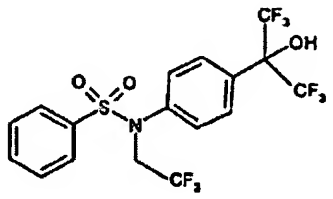
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 and 7-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Shan WO 01/03705 A1.

Shan teaches administering a LXR agonist (as in claim 1) in the treatment of atherosclerotic disease, coronary heart disease (see page 12, lines 10+) as in claims 2 and 4, in a pharmaceutically acceptable carrier (see page 24, lines 7+) as in claim 3.

Shan teaches with regards to claim 7 the formula that identical to that of the instant claimed formula I as shown  (I) (see page 14, lines 1+) wherein the Ar represents an aryl group, R^1 is OH (see page 14, lines 1-12), X (1-6) are

selected from -H (C_1-C_5) etc (see page 15, lines 3+) and Y is $-N(R^{12})S(O)_m$ (see page



15, lines 9+). The reference also teaches the an identical chemical structure as claimed in the instant claim 8.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SVG
7/28/06

Ardin H. Marschel 8/1/06
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SUPERVISORY PATENT EXAMINER